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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,878	12/07/2005	Harry John Wadsworth	PZ0414	2849

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,878	WADSWORTH ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7 and 9-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-7 and 9-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claims 2, 3, 8 and amendment to claims 1, 4, 5 and 9-15, filed on 10/30/2008, is made of record. Claims 1, 4-7 and 9-28 are now pending. In view of applicants' amendment to claim 1, the 102 rejection made in the previous office action has been obviated. However, the following rejections made in the previous office action are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7 and 9-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fluoridation of diphenyliodonium salt, phenyliodonium salt bearing unsubstittuted acetophenone as well as methyl and methoxy substituted acetophenone, does not reasonably provide enablement for any or all iodonium salt and fluoridation any or all aromatic or heteroaromatic compounds generically embraced in claim 1 and compounds with diverse structure embraced in claims 15-18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

In evaluating the enablement question, following factors are considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack

thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to production of aromatic or heteroaromatic fluorine labeled compound by fluoridation of iodonium salt with fluoride in a solvent comprising water. Specification is not adequately enabled for fluoridation of any or all iodonium salt and fluoridation of any or all aromatic or heteroaromatic compounds including those with various reactive functional groups which may be susceptible to the reactions embraced in the process generically embraced in claim 1 and compounds with diverse structure embraced in claims 15-18.

Instant claims recites fluoridation of any iodonium salt but the nucleophilic displacement can occur on both sides of the iodonium salts and if these groups are not aromatic and heteroaromatic, the reaction will not lead to desired product namely fluorinated aryl or heteroaryl. There is no showing in the specification how to one make fluorinated aryl or heteroaryl with such starting materials. Even if one of the group is aryl or heteroaryl there is no guarantee that the reaction would occur to yield fluorinated aryl or heteroaryl. Specification is silent about how to perform the reaction in such cases and arrive at the desired product. In addition, as recited the starting iodonium salt is permitted to be any compound thereby permitting variously substituted iodonium salts. Such a recitation would not exclude reactive groups which may also participate in the said fluoridation reaction. Specification offers no teachings or suggestion as to how to

perform the process of claim 1 in presence of these reactive groups. Specification has no teaching or suggestion as how to make the starting material for the said fluoridation with any substituents including reactive groups. The same is true for the compounds shown in claim 15 and claim 17. There is no teaching of how fluoridation of such compounds are achieved and what starting material is used. Specification offers no teachings or suggestion as to how to perform the process of claim 1 for making these compounds. Note US 2006/0292060 (apparently instant applicants) states:

The use of this reaction in the radiofluoridation of iodonium salts has been reported by Pike et al [1995 J Chem Soc Chem Comm pp2215-16] although with variable radiochemical yield (ROY). The reason for the variability in RCY was not understood. Subsequent reports from the same group [Shah et a11998 J Chem Soc (Perkin Trans 1) 25 pp2043-6 and Martin-Santamaria et a12000 Chem Comm pp649-50] do not offer any further explanation for the variable RCY: More recently, W0st et al [2001 J Labelled Cpd Radiopharm 44 pS12-3] reported that the reaction of phenyliodonium tosylate with [18F] potassium fluoride (in the presence of Kryptofix TM) yielded a very low amount of the desired [18F] codicosteroid. Furthermore, the present applicants have found that radiofluoridation of iodonium salts according to the methods described above produces 5 highly variable RCY (5% to 40%) of the desired [laF] aryl fluoride product. Such lack of reproducibility makes the use of iodonium salts for the synthesis of [18F] aryl fluorides problematic.

Thus, it clear that the fluoridation process is a specialized art with certain degrre of unpredictability. A process which viable for one starting material need not do so for

others. Hence, specification should teach or suggest how to make such compounds with varying structural cores and substituents. Presence of reactive groups would be chemically incompatible the process of fluoridation embraced in the instant claims. Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

2. The predictability or lack thereof in the art:

Hence the process as applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s).

4. The amount of direction or guidance present: Examples illustrated in the experimental section or written description offer no guidance or teachings as to how perform the process of claim 1 when reactive substituents or chemically incompatible substituents are present in the starting material.

5. The presence or absence of working examples:

Although examples specification show the fluoridation process, they are limited to compound with no reactive functionality. There are no representative examples showing the viability of the process for plurality of reactive substituents embraced in the instant claims.

6. The breadth of the claims:

Specification has no support, as noted above, for all compounds generically embraced in the claim language would lead to desired compound of formula I with said reactive groups and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward the aminating agent and halogenating agent embraced in the process claim.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula I embraced in the instant claims.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of reactant- reagent interactions in general, and the lack of working examples regarding the viability of the claimed compounds and processes of making embraced in the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or

use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

This rejection is same as made in the previous office action but now limited to currently pending claims.

Applicants' traversal is not persuasive. As recited applicants' claims are reach through claims. Based on the fluoridation of diphenyliodonium salt, phenyliodonium salt bearing unsubstittuted acetophenone as well as methyl and methoxy substituted acetophenone, instant claims reach through for fluoridation of any or all iodonium salt and fluoridation any or all aromatic or heteroaromatic compounds which are electron deficient. Contrary to applicants' urging this cannot be deemed as objective enablement as the species and genus recited are various largely and each required a distinct process for making the intermediates and there is no guarantee that fluoridation would work on all of them. Furthermore, the radiofluorination is specialized art and required guidance. A radiolabelled material is distinct form unlabelled material. Hence, species claimed in claim 17 requires support in specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-7 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grushin et al.

Grushin et al. teaches a process for fluorination using biphasic system containing water as noted in the above 102 rejection. See entire document especially page 2131.

Instant claims differ from the reference in requiring a water alone or water and miscible solvent for the said reaction.

While Grushin did not teach such a combination of solvent for the said fluoridation reaction, Grushin clearly teaches that for the arylation anions by diphenylhalonium salts use of homogeneous solvent system with water, aqueous alcohols, acetone, dioxane etc. See firs paragraph, page 2130.

Thus, one having ordinary skill in the art at the time of the invention was made would have been motivated to combine teachings of the references and employ the process taught by the prior art to the starting materials and reactants of the instant invention and expect to obtain the desired product because he would have expected the analogous starting materials and reactants react similarly in view of the combine teaching of the prior art. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note In re Kerkhoven 205 USPQ 1069.

See also MPEP 2144.05, which says, under Optimization Within Prior Art Conditions or Through Routine Experimentation:

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence

indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.). See also In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

This rejection is same as made in the previous office action but limited to currently pending claims.

Applicants' argument to overcome this rejection is not persuasive. Grishin clearly teaches that water can be used for such reactions and it is well within skill set of one trained in the art to modify the solvent system as when required for each starting material and reagents.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624